REMARKS

Claims 5-12 are pending in the instant application. By this amendment, Claims 10 and 12 have been amended to clarify the invention, so that the requirement for promotion of whole body health is reflected in the body of the claim. No new matter is added by this amendment. Applicants respectfully request that the amendments and remarks made herein be entered into the record of the instant application.

1. THE REJECTION UNDER 35 U.S.C. § 101 SHOULD BE WITHDRAWN

The claims are rejected under 35 U.S.C. § 101 as lacking utility. The Examiner contends that the disclosed invention is inoperative because no examples are given for such function, so the intended use is not credible.

The present invention relates to methods for using topical oral compositions for promoting and enhancing whole body health or overall systemic health in humans and other animals. The invention is based, in part, on the discovery by the inventors that periodontal infection stimulates a systemic response, including inflammatory and acute immune responses, caused by the spread of oral pathogenic bacteria, associated bacterial toxins and endotoxins and inflammatory cytokines and mediators prompted by these oral pathogens. This infection-stimulated systemic response can result in various diseases and conditions such as cardiovascular disease, stroke, atherosclerosis, diabetes, severe respiratory infections, premature births and low birth weight, post-partum dysfunction in neurologic and developmental functions, and associated increased risk of mortality. These systemic diseases and conditions can be protected against by treating and preventing diseases and conditions of the oral cavity using the methods described and claimed in the instant application.

As evidence that the claimed invention is operable, the Examiner's attention is invited to the Declaration of Dr. Steven Offenbacher, D.D.S., Ph.D., M.MSc. (the "Offenbacher Declaration"), which is attached hereto as Exhibit A. Briefly, the Offenbacher Declaration presents the results of successful experiments to evaluate the efficacy of treating the oral cavity with antimicrobial agents.

The experimental results presented in the Offenbacher Declaration describe the successful use of antimicrobial agents for inhibiting the periodontal infection-induced systemic inflammatory response in an animal model (Offenbacher Declaration ¶ 5). These

assays were carried out following the teaching presented in the instant specification, using standard well-known procedures.

In order to evaluate the efficacy of treatment, an animal model for periodontal infection-induced artherosclerosis was developed (Offenbacher Declaration ¶¶ 6-8). This model mimics a chronic-type inflammatory response to a localized infection similar to that observed in human periodontal disease. In a series of experiments, various dosages of the antimicrobial agents amoxicillin, stannous fluoride, zinc citrate, and cetylpyridinium chloride (CPC) were tested for efficacy at inhibiting systemic inflammatory and acute phase responses that are stimulated by periodontal infection.

These experiments are described in ¶¶ 9, 10 and 11 of the Offenbacher Declaration. Inflammatory and acute phase responses were tested by assaying serum levels of IL-6 and SAA, serum markers for inflammatory response, using standard techniques known in the art such as ELISA, and mouse weight was used as an indicator of overall general health. The results indicate that effective dosages of stannous fluoride, zinc citrate and CPC inhibited the inflammatory response in the experimental group in a dose dependent fashion, whereas untreated animals developed periodontal infection-induced serum acute phase and inflammatory responses and aortic lesions. Moreover, the body weights of the treated animals increased regularly, indicating that the treatments with test compounds protected the mice from adverse consequences of periodontal infection on whole body health.

Thus, as demonstrated by the Offenbacher Declaration the claimed methods for promoting whole body health of the present application are operable and have demonstrated utility.

As such, for the reasons presented above, Applicants respectfully request that the rejection under 35 U.S.C. § 101 be withdrawn.

2. THE REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH, FOR LACK OF WRITTEN DESCRIPTION, SHOULD BE WITHDRAWN

Claims 10-12 are rejected under 35 U.S.C § 112 first paragraph as failing to comply with the written description requirement, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention. Claims 10-12 recite a method that excludes the use of an H2 antagonist as an

additional therapeutic agent. The Examiner asserts that the original disclosure does not describe the concept of the process performed without the use of H2 antagonists, stating that "a negative limitation such as excluding a component requires definitive written description which is not found in the specification."

Applicants respectfully submit that the generic disclosure of additional therapeutic agents and the extensive examples of additional therapeutic agents provided in the instant application supplies sufficient written description support for excluding H2 antagonists, a species within the genus of therapeutic agents. Support for the proposition that claims can be properly amended to exclude a particular species of a genus can be found in § 2173.05(i) of The Manual of Examination Procedure ("M.P.E.P."), 8th Edition, Revision 2, May 2004, which states that "If alternative elements are positively recited in the specification, they may be explicitly excluded in the claims. See *In re Johnson*, 558 F.2d 1008, 1019, 194 U.S.P.Q. 187 (C.C.P.A. 1977), ("[the] specification, having described the whole, necessarily described the part remaining."). See also *Ex parte Grasselli*, 231 USPQ 393 (Bd. App. 1983), aff'd mem., 738 F.2d 453 (Fed. Cir. 1984). The *Johnson* court held that a disclosure of a genus and examples of representative species is sufficient to support a negative limitation in the absence of the limitation in the specification. *Johnson* at 197.

According to *In re Johnson*, "a broad and complete generic disclosure, coupled with extensive examples" constitutes support for removal of species. *Johnson* at 196. In *Johnson*, a genus of polyarylene polyethers, referred to as E´ precursor compounds, is disclosed together with examples that detail numerous species of polyarylene polyethers. "[This] broad *class* [the E´ genus] is identified as embracing suitable *choices* for the E´ precursor compound." Appellants in *Johnson* amended the claims to recite a proviso that removed two of the species, forming a "limited genus." In relation to rejections under § 102 or § 103 (which raised issues under §§ 112 and 120), of the claims containing the proviso, the court held that the "specification supported the claims *in the absence of the limitation*, and that specification, having described the whole, necessarily described the part remaining." [*Emphasis added*] *Id.* at 197.

According to the *Johnson* standard, support for removal of one or more species of - therapeutic agents from a claim would require a complete generic disclosure of therapeutic agents, coupled with an extensive list of examples of such therapeutic agents. Applicants assert that there is sufficient support for removal of one or more species of additional therapeutic agents from Claims 10-12. The specification provides a broad and complete

generic disclosure of such therapeutic agents, as well as extensive examples of compounds that can be used as additional therapeutic agents (see specification at p. 15, *l.* 3-8; p. 29, *l.* 32 - p. 32, *l.* 8 and Claims 5, 6, and 8). The specification discloses numerous species within the genus, such as anti-inflammatory agents including cyclo-oxygenase inhibitors and lipoxygenase inhibitors, metalloproteinase inhibitors, cytokine receptor antagonists, lipopolysaccharide complexing agents, tissue growth factors, immunostimulatory agents, cellular redox modifiers (antioxidants), analgesics, hormones, vitamins, and minerals (see p. 30, *l.* 3-7). The specification states that the antimicrobial agent may be combined with one or more of such therapeutic agents in a single delivery system to provide combined effectiveness (see specification at p. 30, *l.* 8-9). Therefore, the support provided in the instant case for the negative limitation is analogous to the support that the court found acceptable in *Johnson.* Clearly, the specification describes the concept of the process performed without the use of H2 antagonists.

In view of applicable case law and the support provided in the specification, applicants respectfully request the Examiner's withdrawal of the rejection under 35 U.S.C. § 112, first paragraph.

3. THE REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH, FOR LACK OF ENABLEMENT, SHOULD BE WITHDRAWN

Claims 5-12 are rejected for lack of enablement. According to the Examiner, the claims include Markush groups of antimicrobial agents, forms of the product, and H2 antagonists and/or additional therapeutic agents, but the specification fails to teach how to make and use each and every of the components in each of the claimed forms. In addition, with respect to Claim 12, the Examiner contends that, although the specification is enabling for some agents, such as flavors, it does not enable the full scope of "an additional therapeutic agent". Applicants disagree with the enablement rejections for the following reasons.

The test for enablement is whether one of skill in the art could make and use the full scope of the claimed invention without undue experimentation from the disclosure in the patent specification, coupled with information known in the art at the time the patent application was filed. *U.S. v. Teletronics Inc.*, 8 USPQ2d 1217 (Fed. Cir. 1988); *see also In re Wright*, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). The specification preferably omits well-known subject matter. *See Hybritech v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384 (Fed. Cir. 1986)("a patent need not teach, and preferably omits, what is

well known in the art."). Further, the scope of enablement must only bear a reasonable correlation to the scope of the claims. *See In re Fisher*, 166 USPQ 18, 24 (C.C.P.A. 1970); *see also In re Wright*, 27 USPQ2d 1510 (Fed. Cir. 1993). Accordingly, the law does not require the scope of enablement provided by the specification to mirror precisely the scope of protection sought by the claims.

The Examiner alleges that the specification is not enabling for the full scope of "an additional therapeutic agent". However, the Applicants respectfully assert that no undue experimentation is required to make or use therapeutic agents, following the guidance provided in the instant specification and knowledge in the art. As noted above, extensive examples of compounds that can be used as additional therapeutic agents are provided by the specification (*e.g.*, at p. 15, *l.* 3-8; p. 29, *l.* 32 - p. 32, *l.* 8 and Claims 5, 6, and 8). Such therapeutic agents are readily available in the art, and the skilled person would know how make and use such agents without undue experimentation. Such routine tests may be used according to test the efficacy of the claimed methods at promoting whole body health. Moreover, the Offenbacher Declaration demonstrates that such routine tests may be used to practice the full breadth of the claimed methods without having to resort to undue experimentation.

In view of the disclosure in the instant specification and the level of skill in the art, applicants respectfully request the Examiner's withdrawal of the rejection under 35 U.S.C. § 112, first paragraph, for lack of enablement.

4. THE REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH, FOR INDEFINITENESS, SHOULD BE WITHDRAWN

Claims 5-12 are further rejected under 35 U.S.C. § 112, second paragraph, for indefiniteness.

First, the Examiner contends that Claim 5 is indefinite because the terms "zinc ion agent" and "copper ion agent" are unclear because it is not understood what the term "agent" is intended to mean. Applicants disagree, and submit that the term agent is used in the specification in accordance with its common meaning, and the person skilled in the art would clearly understand this term. An "agent" is defined as "An active force or substance capable of producing an effect" according to Stedman's Medical Dictionary (see Exhibit B, page 36 of Stedman's Medical Dictionary 26th Edition). Thus the skilled artisan would clearly

understand a "zinc ion agent" and a "copper ion agent" to mean a substance capable of producing a zinc ion and a copper ion, respectfully. Such substances or agents are generally in the form of salts, such as copper bisglycinate, copper glycinate, zinc citrate, and zinc lactate (see specification, p. 14, *l.* 25).

The Examiner further contends that Claim 10 is indefinite because it is not clear what the amount is safe and effective for. In response, Claim 10 has been amended to clarify that the amount of antimicrobial agent is effective to promote whole body health. It is now clear that the claimed effective amount can be determined by the skilled artisan from the description provided by the specification, and is thus definite under the applicable case law. *In re Halleck*, 422 F.2d 911, 164 USPQ 647 (CCPA 1970) ("Where an amount is not critical and those skilled in the art would be able to determine from the written disclosure, including the examples, what an effective amount is). Thus, Claim 10, as amended, is definite.

Finally, the Examiner contends that Claim 12 is indefinite because "an additional therapeutic agent" is indefinite. Applicants disagree, and submit that "therapeutic agent" is a commonly used term with a clear and definite meaning. The term "therapeutic agent" is commonly understood by the skilled artisan. Merriam-Webster's Dictionary defines "therapeutic" as "of or relating to the treatment of disease or disorders by remedial agents or methods" (see Exhibit C, page 1223 of Merriam-Webster's Collegiate Dictionary 10th Edition). As noted above, the person skilled in the art would clearly understand the meaning of the term agent. Stedman's Medical Dictionary defines the term "therapeutic" to mean "relating to therapeutics or to the treatment, remediating, or curing of a disorder or disease." (see Exhibit B, page 1798 of Stedman's Medical Dictionary 26th Edition). Thus, the skilled person would understand an "additional therapeutic agent" to mean a substance capable of producing a therapeutic effect, in addition to the antecedent antimicrobial agent. As noted above, the specification provides extensive examples of such therapeutic agents, including for example, anti-inflammatory agents (including cyclo-oxygenase inhibitors and lipoxygenase inhibitors), H2 antagonists, metalloproteinase inhibitors, cytokine receptor antagonists, lipopolysaccharide complexing agents, tissue growth factors, immunostimulatory agents, cellular redox modifiers (antioxidants), analgesics, hormones, vitamins, and minerals (see specification at p. 29, *l.* 32 - p. 32, *l.* 8).

For the foregoing reasons, applicants respectfully request the Examiner's withdrawal of the rejection under 35 U.S.C. § 112, second paragraph, for indefiniteness.

5. THE REJECTION UNDER 35 U.S.C. § 102(b) IS IN ERROR AND SHOULD BE WITHDRAWN

Claims 5 to 9 are rejected under 35 U.S.C. § 102(b) as anticipated by Singer, as decided by the Board of Appeals in its decision of 3/26/04. Singer teaches a method or treatment of gingivitis or periodontitis comprising the topical administration of the oral cavity of a composition comprising an H2 antagonist and, optionally, an antimicrobial anti-plaque agent and a pharmaceutically acceptable carrier.

The claims under appeal recited methods for promoting whole body health in human and other animal subjects comprising the topical administration of a composition comprising an antimicrobial agent, an H2 antagonist and a pharmaceutically acceptable carrier. The Appeal Board rejected the claims under appeal, holding that the purported new use of promoting whole body health did not constitute a patentable difference because the preamble offered no distinct definition of the claimed inventions limitations. The amended claims obviate this rejection.

Claims 5 to 9 have since been amended so that the claims require the use of an amount of antimicrobial agent (in Claims 5 to 7), or the amount of antimicrobial agent and the therapeutic agent (in Claims 8 and 9) are effective to promote whole body health. Thus, the method requires the step of topically administering to the oral cavity of a human or animal subject a composition comprising an amount of antimicrobial agent effective to promote whole body health. This step is not disclosed in Singer, and is thus a patentable limitation not present in the prior art.

Under Section 102(b), in order for a prior art reference to serve as an anticipatory reference of a claim, the reference must disclose every element of the claim, either implicitly or explicitly (see *In re Schreiber* 128 F.3d 1473, 1477, 44 USPQ2d 1429, 142 (F.Cir. 1997). A finding of inherency further requires that practicing the prior art method would necessarily and inevitably result in the claimed invention, *i.e.*, promotion of whole body health.

The Examiner regards the issue of inherent anticipation by Singer as "the issue already decided by the Board of Appeals regarding the inherency of promoting whole body health" (at page 5, line 13, of the Office Action). It should be noted, however, that the Board's determinations were made with respect to the rejected claims, not the currently pending claims. There is no evidence on the record to support the Examiner's conclusion that practicing the method of Singer inevitably requires the step of topically administering to the

oral cavity of a human or animal subject a composition comprising an amount of antimicrobial agent effective to promote whole body health, a required element of Claims 5 to 9, as amended. Thus, Singer does not inherently anticipate the invention as claimed in amended Claims 5 to 9.

The Examiner also contends that the phrase "promoting whole body health" is meaningless in context, asking whether such acts as breathing air, drinking water, or brushing teeth promote whole body health. Clearly this is not the case. Promoting "whole body health" refers to improving overall systemic health, which is characterized by reducing systemic inflammatory and acute responses, resulting in the reduction in risk of development of major systemic diseases and conditions including cardiovascular disease, stroke, diabetes, severe respiratory infections, premature births and low birth weights, and associated risk of mortality. Improvement in whole body health is measurable, and routine assays for measuring systemic inflammatory and acute responses are well known in the art. Such routine assays are available to test the effect of antimicrobial agents on serum markers of systemic inflammatory responses and acute response. The Offenbacher Declaration demonstrates the use of such assays, and the efficacy of antimicrobial agents in the claimed methods for promoting whole body health. Clearly, "breathing air" or "drinking water" would not demonstrate effectiveness in such assays.

The Examiner takes the position that the nexus between dental disease and illness, disability and death would highly likely to be well known. The Examiner asserts that it would be likely that humans in contact with animals would be aware of the connection between oral infection, loss of teeth, loss of oral function and the attendant risk to health of the animals. However, this supposition does not meet the standard for anticipation under 35 U.S.C. § 102(b). As noted above, under Section 102(b), an anticipatory reference must disclose every element of the claim, either implicitly or explicitly (*In re Schreiber* at 1477). There is no reference of record in this case that discloses the effect of periodontal infection on systemic disease or inflammatory response. Thus, there is no evidence on the record of a prior art reference that satisfies the standard for anticipation under Section 102(b).

Therefore, applicants believe the rejection under 35 U.S.C. § 102(b) is in error, and respectfully request its withdrawal.

7. THE REJECTION UNDER 35 U.S.C. § 103(a) IS IN ERROR AND SHOULD BE WITHDRAWN

Claims 10 to 12 are rejected under 35 U.S.C. § 103(a) as rendered obvious in view of Singer. The Examiner contends that it would have been obvious to the skilled artisan to make oral care products containing components described by Singer without H2 antagonists. Applicants disagree for the reasons set forth below.

A finding of obviousness under 35 U.S.C. §103 requires a determination of: (1) the scope and content of the prior art; (2) the level of ordinary skill in the art; (3) the difference between the claimed subject mater and the prior art; and (4) whether the differences are such that the subject matter as a whole would have been obvious to one of ordinary skill in the art at the time the invention was made. *Graham v. Deere* 383 U.S. 1 (1966). The relevant inquiry is whether the prior art suggests the invention, and provides one of ordinary skill in the art with a reasonable expectation of success. *In re O'Farrell*, 853 F.2d 894, 903 (Fed. Cir. 1988).

Both the suggestion and the reasonable expectation of success must be found in the prior art. *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991). The prior art must either expressly disclose every claim limitation or suggest modifications to meet every claim limitation. *Litton Indus. Products, Inc. v. Solid State Systems*, 755 F.2d 158, 164 (Fed. Cir. 1985). In *Litton*, the District Court found that a device was obvious by focusing on what "it thought was the 'most critical feature.'" The Federal Circuit reversed this decision because the cited references neither taught specific claim elements nor suggested to one of ordinary skill in the art the necessary modifications.

According to the Examiner, it would have been obvious to one of ordinary skill in the art to make oral care products as described by Singer without H2 antagonists because oral care products not containing H2 antagonists were known at the time of the invention.

Claims 10 -12 have been amended so that the claims require that (i) the compositions used do not include an H2 antagonist, and that (ii) the amounts used are effective to promote whole body health.

Singer teaches the use of H2 antagonists for treatment of gingivitis or periodontitis, the critical feature of the method being the use of H2 antagonists. Nothing in Singer suggests removing the H2 antagonists, a required element of the claim. Moreover, Singer does not teach or suggest a method comprising a step of topically administering a composition

comprising an amount of an antimicrobial agent and a pharmaceutical carrier effective for promoting whole body health. Thus, even if the H2 antagonist were removed, as the Examiner suggests, there is no suggestion in Singer or any other prior art to use an amount that is effective to promote whole body health, a required element of the claim.

Thus, there is no reference, or any combination of references, of record in this case that discloses the claimed methods for use of antimicrobial agents for treating periodontal infection to achieve the desired effect on systemic disease or whole body health. Thus, there is no evidence on the record of a prior art reference or combination of references that satisfy the standard for anticipation under Section 103.

In view of the foregoing, Applicants submit that the rejection for obviousness under 35 U.S.C. §103(a) should be withdrawn.

CONCLUSION

In light of the amendments and remarks above, Applicants estimate that the pending claims are allowable. Applicants respectfully request that the foregoing amendments and remarks in be made of record in the instant application.

Respectfully submitted,

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